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Attorney Docket No.: QUIG-1006USCIP



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Richard Rosenbloom

U.S. Application No.: 10/045,790

Filed: January 14, 2002

For: ORAL COMPOSITIONS AND
METHODS FOR THE
PREVENTION, REDUCTION
TREATMENT OF RADIATION
INJURY

Group Art Unit: 1617

Examiner: Shaojia A. Jiang

#14
9-15-03
Shaojia A. Jiang

DECLARATION OF ANTHONY W. ADDISON PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner of Patents & Trademarks
Washington, D.C. 20231

Sir:

1. I, Anthony W. Addison, Ph. D., hereby declare as follows:

2. I am a Professor of Chemistry at Drexel University in Philadelphia, Pennsylvania.

My detailed *curriculum vitae* is attached hereto as Exhibit A.

3. I have reviewed the specification, drawings and original claims of U.S. patent application no. 10/045,790, as well as the currently-pending claims of U.S. patent application no. 10/045,790 (hereinafter, "the '790 application"). I have also reviewed the Office Action mailed on October 16, 2002, the Applicant's response thereto mailed

on January 2, 2003, and the Final Rejection mailed on March 26, 2003 (hereinafter "the Final Rejection").

I. Written Description Under 35 U.S.C. §112, First Paragraph

A. The Standard

4. It is my understanding that in the Final Rejection, the Examiner has taken the position that the use of the terms, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation," "one or more antioxidants," "one or more antioxidant enzymes," and "anti-inflammatories," in the claims of the '790 application, do not meet the written description requirement under 35 U.S.C. §112, first paragraph.

5. It is my understanding that in Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) (rehearing *en banc* denied), the Court of Appeals for the Federal Circuit adopted the following standard from U.S. Patent and Trademark Office Written Description Guidelines for determining whether the written description requirement of 35 U.S.C. §112, First Paragraph, has been met,

"The written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics... i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and

structure, or some combination of such characteristics.” Guidelines, 66 Fed. Reg. at 1166.

See Enzo Biochem, 296 F.3d at 1324.

6. It is also my understanding that the written description requirement of 35 U.S.C. §112, First Paragraph, for a claimed genus, “may be satisfied through sufficient description of a representative number of species by actual reduction to practice, ...” MPEP §2163, II,A.3(a)(ii) and *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, “Written Description” Requirement*, 66 Fed.Reg. 1099, 1106 (Jan. 5, 2001).

7. It is also my understanding that the U.S. Patent and Trademark Office Written Description Guidelines provide that,

A ‘representative number of species’ means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. What constitutes a ‘representative number’ is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a ‘representative number’ depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. Description of a representative number of species does not require the description to be of such

specificity that it would provide individual support for each species that the genus embraces.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed.Reg. 1099, 1106 (Jan. 5, 2001).

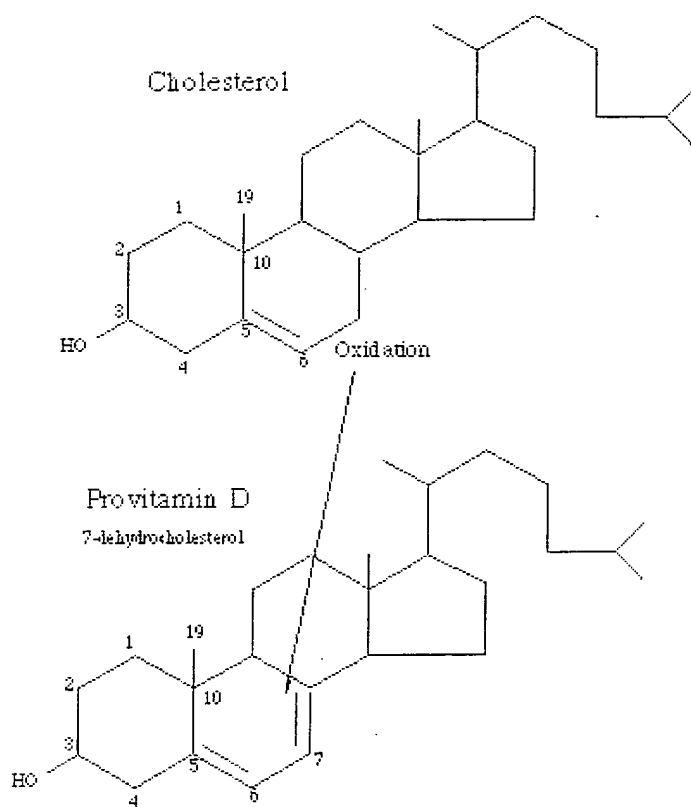
B. Support for the Terminology, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation"

8. The specification of the '790 application discloses that the methods which are the subject of the claims of the '790 application may employ compositions including one or more compounds effective to regulate or inhibit at least one of cell differentiation and cell proliferation. See e.g. page 3, lines 3-6, page 17, lines 22-26 and original claim 1. Thus, there is a literal disclosure of the use of this genus of compounds in the '790 application as originally filed.

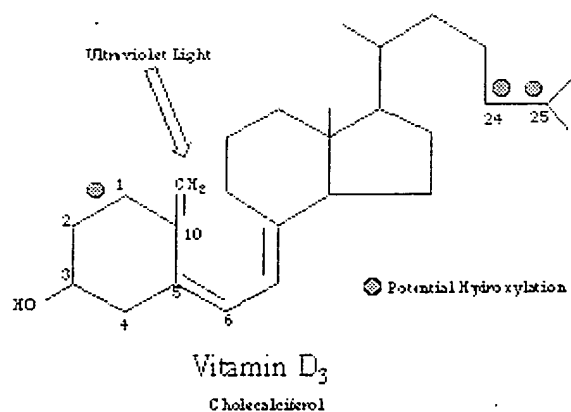
9. The specification of the '790 application also discloses exemplary compounds effective to regulate or inhibit at least one of cell differentiation and cell proliferation at pages 3-5 of the '790 application as originally filed. The relevant disclosure is as follows:

Exemplary compounds that regulate cell differentiation and/or cell proliferation are vitamin D₃, vitamin D₃ analogs, compounds that may be converted or metabolized into vitamin D₃ in the human body, and metabolites thereof. Exemplary compounds that may be converted or metabolized into vitamin D₃ include common cholesterol illustrated below. The cholesterol illustrated below may be converted into Provitamin D when a hydrogen is removed from the number 7 carbon, which then

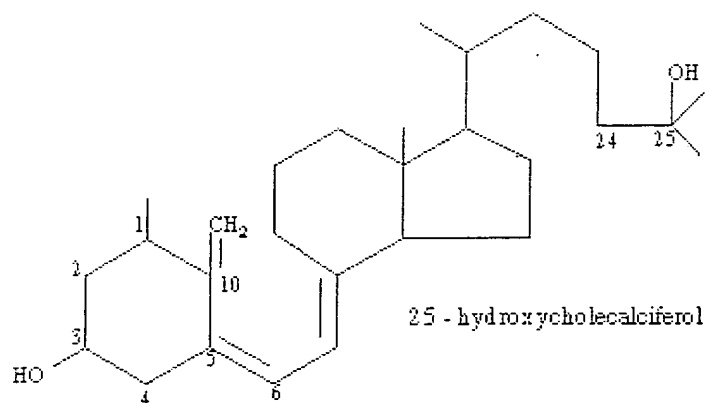
forms a double bond with the number 8 carbon, in the second, or 'B' ring of the cholesterol molecule. The cholesterol is 'oxidized' (that is, an electron is removed with the hydrogen atom), so that the double bond is a consequence of 2 mutually shared electrons between carbons 7 and 8.



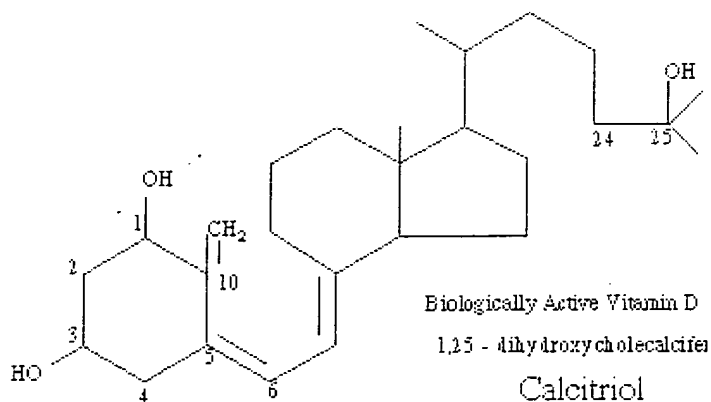
Provitamin D may be converted to Vitamin D₃ by the action of ultraviolet light through human skin. In this reaction, the B ring of the sterol molecule is opened.



Cholecalciferol, which is Vitamin D₃, may be further converted into another vitamin D intermediate, 25-hydroxycholecalciferol, in the liver by mitochondrial hydroxylase, in the presence of NADPH, and molecular oxygen.



When more active vitamin D₃ is required, 25-hydroxycholecalciferol is transported to the kidney where a new hydrolase enzyme is synthesized. This enzyme introduces another hydroxyl group at position 1, and the bioactive form of Vitamin D₃, calcitriol, is produced.



Exemplary vitamin D₃ analogs include 1(S), 3(R)-dihydroxy-20(R)-(1-ethoxy-5-ethyl-5-hydroxy-2-heptyn-1-yl)-9, 10-seco-pregna-5(Z), 7(E), 10(19)-triene. Exemplary vitamin D₃ metabolites include 1, 25-dihydroxyvitamin D₃. Also, pharmaceutically acceptable salts of the compounds that regulate cell differentiation and/or cell proliferation may be employed.

10. From a review of the foregoing information, it is my opinion as a skilled chemist that the specification of the above-identified application discloses a representative number of species which is sufficient for a skilled chemist to recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of compounds that regulate or inhibit cell differentiation and cell proliferation.

11. This conclusion is based, in part, on the fact that the level of knowledge and skill in the art is relatively high, as is evidenced by the fact that tests for determining whether a particular compound regulates or inhibits one or more of cell differentiation and cell proliferation are commercially available. For example, DiscoverX Corporation of Fremont, CA markets a Hithunter™ tyrosine kinase assay to detect inhibitors of tyrosine kinase and tyrosine phosphatase, which control or regulate cellular growth, proliferation and differentiation using β -galactosidase EFC activity. See the article from DiscoverX Corporation attached as Exhibit B.

C. Support for the Terminology, "one or more antioxidants"

12. I am aware that since 1976, at least 5281 United States patents have been issued using either the term, "antioxidant" or the term, "antioxidants" in the claims. A copy of the search results from the U.S. Patent Office database confirming this is attached hereto as Exhibit C.

13. The specification of the '790 application discloses that methods which are the subject of the claims of the '790 application may employ compositions including one or more antioxidants. See e.g. page 7, lines 4-14, page 17, lines 22-26 of the '790 application as originally filed, and original claim 1 of the '790 application. Thus, there is a literal disclosure of the use of the genus of antioxidants in the '790 application as originally filed.

14. The specification of the '790 application also discloses exemplary antioxidants at page 7, lines 14-22 of the original application. The relevant disclosure is as follows:

Preferred antioxidants are selected from ascorbic acid (vitamin C) and its esters, for example, ascorbyl palmitate; vitamin A and its esters, for example, vitamin A palmitate; vitamin E and its esters, for example, vitamin E acetate; α -lipoic acid, especially DL- α -lipoic acid; carotenoids such as β -carotene; chlorophyllin and its salts; coenzyme Q10; glutathione; green tea polyphenols, such as (-)-epigallocatechin-3-gallate; catechin; galangin; rutin; luteolin; morin; fisetin; silymarin; apigenin; ginkgolides; hesperitin; cyanidin; citrin; curcuminoids and structurally similar derivatives thereof which exhibit antioxidant activity. Even more preferably, mixtures of two or more antioxidants are employed in the composition of the present invention.

15. From a review of the foregoing information and my general knowledge of chemistry, it is my opinion as a skilled chemist that the specification of the '790 application as originally filed, disclosed a representative number of species which is sufficient for a skilled chemist to recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of antioxidants at the time the '790 application was filed, thereby satisfying one of the tests from the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph that was approved for use in the Enzo Biochem decision cited above.

16. This conclusion is based, in part, on the fact that the level of knowledge and skill in the art is relatively high, as is evidenced at least by the following:

- A. Persons of ordinary skill in the art are aware from publications that there are numerous compounds that are antioxidants.
- B. Persons of ordinary skill in the art of chemistry are well aware that there is a known correlation between the function of a compound as an antioxidant and the structure of a chemical compound. One large class of these antioxidants, are those which are conjugated polycyclic or aromatic molecules, which through their ability to act as reducing agents, perform as scavengers of

oxidizing free radicals.

- C. Persons of ordinary skill in the art of chemistry are aware of tests which can be used to determine if a particular chemical compound has antioxidant activity, such as those described or referenced in "A Rapid Gas Chromatographic Assay for Determining Oxyradical Scavenging Capacity of Antioxidants and Biological Fluids," Winston, G.W., et al., *Free Radical Biology & Medicine*, Vol. 24, No. 3, pp. 480-493, (1998) (Exhibit D hereto) and "Protein Protection by Antioxidants: Development of a Convenient Assay and Structure-Activity Relationships of Natural Polyphenols," Salvi, A., et al., *Helvetica Chimica Acta*, Vo. 85 (2002) (Exhibit E hereto).
- D. At least 5281 United States patents have issued since 1976 using the term, "antioxidant" or "antioxidants" in the claims of the patent.
- E. The term, "antioxidant" is a commonly used, well-known term in the art of chemistry as is evidenced by the fact that the term can be found in the dictionary.
- F. The term, "antioxidant" has been defined in detail in an earlier published patent application WO 0057876 A1, published on October 5, 2000 (Exhibit F).

17. There are known correlations between antioxidant activity and particular chemical structures. One large class of these antioxidants, are those which are conjugated polycyclic or aromatic molecules, which through their ability to act as reducing agents, perform as scavengers of oxidizing free radicals. It is my opinion that the disclosure of the '790 application, taken together with the known structural correlations, is sufficient to demonstrate that the applicant had possession of the necessary common attributes or features of the elements possessed by the members of the genus of antioxidants at the time the application was filed, thereby satisfying a second one of the tests found in the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph that was approved in the Enzo Biochem decision cited above.

18. I have also reviewed U.S. Patent no. 5,747,026 ("the '026 patent), which was issued on May 5, 1998, a copy of which is enclosed as Exhibit G. The '026 patent uses the term, "antioxidant" in method claim 1. The only antioxidant that appears to be disclosed in the '026 patent is the antioxidant enzyme superoxide dismutase.

19. I am aware that the requirements of 35 U.S.C. §112, first paragraph, must be met prior to the issuance of a United States Patent. Therefore, based on the fact that the '026 patent was issued by the U.S. Patent and Trademark Office, claim 1 of the '026 patent is presumed to satisfy the requirements of 35 U.S.C. §112, first paragraph.

20. Comparing the disclosure of the '790 application relating to "antioxidants" to the disclosure of the '026 patent relating to "antioxidants," it is my conclusion that the '790 application contains significantly more disclosure relating to antioxidants than the '026 patent. Moreover, the '790 application also contains a much longer list of the various species of antioxidants that may be employed, than is found in the '026 patent. In fact, the '026 patent mentions only superoxide dismutase as a species of antioxidant, whereas the '790 application mentions at least 25 species of antioxidant, in addition to mentioning superoxide dismutase.

21. Accordingly, it is my conclusion that since the disclosure of the '026 patent was sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for the term, "antioxidant", then the substantially more extensive disclosure of the '790 application must certainly be sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for the term, "antioxidant."

D. Support for the Terminology, "one or more antioxidant enzymes"

22. I am aware that since 1976, 5281 United States patents have been issued using either the term, "antioxidant" or the term, "antioxidants" in the claims.

23. The specification of the '790 application discloses that the methods which are the subject of the claims of the '790 application may employ compositions including one or more antioxidants. See e.g. page 7, lines 4-14, page 17, lines 22-26 of the '790

application as originally filed, and original claim 1 of the '790 application. The specification of the '790 application also discloses that the one or more antioxidants may include one or more antioxidant enzymes. See page 8, lines 1-20 of the '790 application as originally filed. Thus, there is a literal disclosure of the use of this genus of antioxidant enzymes in the '790 application as originally filed.

24. The specification of the '790 application also discloses exemplary antioxidant enzymes at page 8, lines 4-6 of the '790 application as originally filed. The relevant disclosure is as follows:

The preferred antioxidant enzymes useful in the present invention include superoxide dismutase, catalase, glutathione peroxidase and methionine reductase.

25. From a review of the foregoing information and my general knowledge of chemistry, it is my opinion as a skilled chemist that the specification of the '790 application, as originally filed, disclosed a representative number of species which is sufficient for a skilled chemist to recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of antioxidant enzymes, at the time the '790 application was filed, thereby satisfying one of the tests from the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph that was approved for use

in the Enzo Biochem decision cited above.

26. This conclusion is based, in part, on the fact that the level of knowledge and skill in the art is relatively high, as is evidenced at least by the following:

- A. Persons of ordinary skill in the art of chemistry are aware of the existence of several antioxidant enzymes.
- B. Persons of ordinary skill in the art of chemistry are aware of assays which can be used to determine if a particular enzyme has antioxidant activity, some examples of which are listed in, "Oxidative Stress Assay Kits," (Exhibit H) and U.S. Patent no. 6,429,021 (Exhibit I).
- C. The '026 patent (Exhibit G), issued on May 5, 1998 claiming an antioxidant enzyme in claim 2.
- D. The term, "antioxidant" is a commonly used, well-known term in the art of chemistry as is evidenced by the fact that the term can be found in numerous dictionaries.

27. It is also my opinion that the disclosure of the '790 application as originally filed, taken together with the known assays and the known antioxidant enzymes, is sufficient to demonstrate that the applicant had possession of the necessary common attributes

or features of the elements possessed by the members of the genus of antioxidant enzymes at the time the '790 application was filed, thereby satisfying a second one of the tests from the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph that was approved for use in the Enzo Biochem decision cited above..

28. The '026 patent (Exhibit G) claims "antioxidant enzymes" in method claim 2. The only antioxidant or antioxidant enzyme that appears to be disclosed in the '026 patent is the antioxidant enzyme superoxide dismutase.

29. I am aware that the requirements of 35 U.S.C. §112, first paragraph, must be met prior to issuance of a United States Patent. Therefore, based on the fact that the '026 patent was issued by the U.S. Patent and Trademark Office, claim 2 of the '026 patent must satisfy the requirements of 35 U.S.C. §112, first paragraph.

30. Comparing the disclosure of the '790 application to the disclosure of the '026 patent relating to "antioxidant enzymes," it is my conclusion that the '790 application contains significantly more disclosure than the '026 patent relating to antioxidants, and a longer list of the various species of antioxidant enzymes that may be employed, than the '026 patent. In fact, the '026 patent mentions only superoxide dismutase as a species of antioxidant enzyme, whereas the '790 application mentions three species of

antioxidant enzyme, in addition to mentioning superoxide dismutase. Accordingly, it is my conclusion that since the disclosure of the '026 patent was sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for claiming, "antioxidant enzymes", then the substantially more extensive disclosure of the '790 application must certainly be sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for the term, "antioxidant enzyme."

E. Support for the Terminology, "Anti-inflammatories"

31. I am aware that at least 2936 United States patents have been issued since 1976 containing the word, "anti-inflammatory" in the claims of the patent. A copy of the search results from the U.S. Patent and Trademark Office database confirming this is attached as Exhibit J. I am also aware that an additional 186 United States patents have been issued since 1976 containing the word, "anti-inflammatories" in the claims of the patent. A copy of the search results from the U.S. Patent and Trademark Office database confirming this is attached as Exhibit K.

32. The specification of the '790 application discloses that the methods which are the subject of the claims of the '790 application may employ compositions including anti-inflammatories. See e.g. page 16, lines 21-23, and page 17, line 20 of the '790 application as originally filed, and original claim 12 of the '790 application. Thus, there was a literal disclosure of the use of the genus of anti-inflammatories in the '790

application as originally filed. The '790 application as originally filed also disclosed an example of an anti-inflammatory, namely, γ -linolenic acid. See page 20, line 6 of the '790 application as originally filed.

33. I am aware that the United States Food and Drug Administration ("FDA") defines anti-inflammatories as drugs used to reduce inflammation – the redness, heat, swelling, and increased blood flow found in infections and in many chronic non-infective diseases such as rheumatoid arthritis and gout. See "Analgesia and Anti-Inflammatory Drug Information" from the U.S. Food and Drug Administration Center for Drug Evaluation and Research (Exhibit L). I am also aware that the FDA maintains a list of approved anti-inflammatory drugs. See Exhibit L.

34. From a review of the foregoing information and my general knowledge of chemistry, it is my opinion as a skilled chemist that the specification of the '790 application, as originally filed, disclosed information sufficient for a skilled chemist to recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus of anti-inflammatories, at the time the '790 application was filed, thereby satisfying one of the tests from the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph, that was approved for use in the Enzo Biochem decision cited above.

35. This conclusion is based, in part, on the fact that the level of knowledge and skill in the art is relatively high, as is evidenced at least by the following:

- A. Persons of ordinary skill in the art of chemistry are aware of the existence of numerous anti-inflammatories.
- B. Persons of ordinary skill in the art of chemistry are aware that the FDA has a list of approved anti-inflammatories.
- C. At least 3112 United States patents have been issued since 1976 using at least one of the words, "anti-inflammatory" or "anti-inflammatories" in the claims.
- D. Persons of ordinary skill in the art of chemistry are aware that there are known correlations between the function of a compound as an anti-inflammatory and the structure of a chemical compound.
- E. The term, "anti-inflammatory" is a commonly used, well-known term in the art of chemistry as is evidenced by the fact that a definition of the term can be found on the FDA web site and that the term can be found in numerous dictionaries.

36. There are known correlations between anti-inflammatory activity and particular

chemical structures as evidenced by, "Quantitative Structure – Activity Relationship (QSAR) Studies on Non Steroidal Anti-Inflammatory Drugs (NSAIDs)," Hadjipavlou-Litina, Dimitra, *Current Medicinal Chemistry*, 2000, 7, 375-388 (Exhibit M). Exhibit M shows that there are several classes of compounds that are known to have anti-inflammatory activity. As a result of this knowledge, skilled persons have confidence that similar compounds having small variations in the chemical structure will also perform as anti-inflammatories.

37. Two examples of skilled persons making small changes in structure to known anti-inflammatories to obtain additional compounds having anti-inflammatory activity are found in "Three-Dimensional Quantitative Structural Activity Relationship (3D-QSAR) Studies of Some 1,5-Diarylpyrazoles: Analogue Based Design of Selective Cyclooxygenase-2 Inhibitors," Desiraju, G.R., et al., *Molecules* 2000, 5, 945-955 (Exhibit N), and "Structure-Activity Relationship in Nonsteroidal Antiinflammatory Agents, Including QSAR in Fenamate Derivatives," Bekemeier, H., et al., *Agents Actions Suppl.*, vol. 10, pp. 17-34 (1982) (Exhibit O). The foregoing information demonstrates that there is a high level of skill and knowledge regarding chemical structures that produce anti-inflammatory activity. Therefore, it is my opinion that the disclosure of the '790 application, taken together with the known structural correlations, is sufficient to demonstrate that the applicant had possession of the necessary common

U.S. Application No.: 10/045,790

attributes or features of the elements possessed by the members of the genus of anti-inflammatories at the time the application was filed, thereby satisfying a second one of the tests found in the U.S. Patent Office Written Description Guidelines for meeting the requirements of 35 U.S.C. §112, first paragraph that was approved in the Enzo Biochem decision cited above.

38. I have also reviewed U.S. Patent no. 6,465,003 B2 ("the '003 patent"), which was issued on October 15, 2002 (Exhibit P). The '003 patent uses the term, "anti-inflammatories" in method claim 4. The only disclosure relating to anti-inflammatories that appears in the specification of the '003 patent appears to be at column 8, lines 29-34 of the '003 patent where it is disclosed that a variety of different medicaments can be placed in the coating, and that such medicaments may include anti-inflammatories.

39. I am aware that the requirements of 35 U.S.C. §112, first paragraph, must be met prior to the issuance of a United States Patent. Therefore, based on the fact that the '003 patent was issued by the U.S. Patent and Trademark Office, claim 4 of the '003 patent is presumed to satisfy the requirements of 35 U.S.C. §112, first paragraph.

40. Comparing the disclosure of the '790 application relating to "anti-inflammatories" to the disclosure of the '003 patent relating to "anti-inflammatories," it is my conclusion that the '790 application contains at least the same amount of disclosure relating to

anti-inflammatories than the '003 patent. Moreover, the '790 application also contains a specific example of a species of anti-inflammatory that may be employed, namely, γ -linolenic acid. The '003 patent does not appear to mention any species of anti-inflammatory in the specification.

41. Accordingly, it is my conclusion that since the disclosure of the '003 patent was sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for the term, "anti-inflammatories," then the more extensive disclosure of the '790 application, which includes a specific example of an anti-inflammatory, must certainly be sufficient to meet the requirements of 35 U.S.C. §112, first paragraph, for the term, "anti-inflammatories."

II. Definiteness Under 35 U.S.C. §112, Second Paragraph

42. It is my understanding that,

If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. §112, second paragraph would be appropriate.

MPEP §2173.02 citing *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993). Thus, it follows that if a person of ordinary skill in the art is able to interpret the metes and bounds of the claim so as to understand how to avoid infringement, the claim meets the requirements of 35 U.S.C. §112, second paragraph.

A. One or More Antioxidants

43. Upon review of the '790 application as originally filed, taken in combination with my common general knowledge and my knowledge of the prior art, it is my conclusion that a person of ordinary skill in the art of chemistry is able to determine the metes and bounds of the term, "one or more antioxidants." This conclusion is based on at least the following facts:

- A. Since 1976, at least 5281 United States patents have been issued using the words "antioxidant" or "antioxidants" in the claims.
- B. Numerous antioxidants are known to persons skilled in the art.
- C. At least 25 different antioxidants are specifically listed in the '790 application.
- D. Routine tests exist for determining whether a compound has antioxidant activity, as evidenced by Exhibits H and I hereto, and thus a person of ordinary skill in the art can simply take a specific compound and test it for antioxidant activity to determine whether that compound falls within the metes and bounds of the claims.
- E. In my experience, persons of ordinary skill in the art are capable of

determining whether a particular chemical compound exhibits antioxidant activity and therefore is an antioxidant.

B. One or More Antioxidant Enzymes

44. Upon review of the '790 application as originally filed, taken in combination with my common general knowledge and my knowledge of the prior art, it is my conclusion that a person of ordinary skill in the art of chemistry is able to determine the metes and bounds of the term, "one or more antioxidant enzymes." This conclusion is based on at least the following facts:

- A. At least United States patent no. 5,747,026 (Exhibit G) has been issued claiming "antioxidant enzymes" in claim 2.
- B. Several antioxidant enzymes are known to persons skilled in the art.
- C. Several antioxidant enzymes are listed in the '790 application.
- D. Routine assays exist for determining whether a chemical compound or an enzyme has antioxidant activity, a few examples of which are listed in Exhibits H and I hereto. Thus a person of ordinary skill in the art can simply take a specific enzyme and test it for antioxidant activity using a routine test to determine whether the compound falls within the metes and bounds of the

claims.

C. Anti-Inflammatories

45. Upon review of the '790 application as originally filed, taken in combination with my common general knowledge and my knowledge of the prior art, it is my conclusion that a person of ordinary skill in the art of chemistry is able to determine the metes and bounds of the term, "anti-inflammatories." This conclusion is based on at least the following facts:

- A. Since 1976, at least 3112 United States patents have been issued using the words "anti-inflammatory" or "anti-inflammatories" in the claims,
- B. Numerous anti-inflammatories are known to persons skilled in the art,
- C. Persons of ordinary skill in the art of chemistry are aware that there are known correlations between the function of a compound as an anti-inflammatory and the structure of a chemical compound (See e.g. Exhibits M, N and O).
- D. The term, "anti-inflammatory" is a commonly used, well-known term in the art of chemistry as is evidenced by the fact that a definition of the term can be found on the FDA web site and that the term can be found in numerous

dictionaries.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that the statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated:

6 Aug 2003

Respectfully submitted

By:



Anthony W. Addison, Ph.D.